

Surgical Treatment for Carcinoma of the Thoracic Esophagus With Major Involvement in the Neck or Upper Mediastinum

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Background and Objectives: In carcinoma of the thoracic esophagus, most surgeons consider that esophagectomy is contraindicated in patients with clinical evidence of major extraesophageal involvement in the lower neck or peritracheal regions. However, metastases to these regions are commonly found even in early phases of carcinoma invasion. With recent progress in preoperative assessment, operative technique and adjuvant therapy, esophagectomy could possibly benefit appropriately selected patients.

Methods: We retrospectively analyzed results in 42 patients who had major involvement in the neck or upper mediastinum and who underwent esophagectomy with systematic lymph node dissection. We operated upon patients unless lesions were assessed as definitely unresectable. Preoperatively, 32 had enlarged peritracheal nodes greater than 15 mm in diameter on computed tomography, 18 had hard unmobile tumors in the lower neck, 9 had recurrent laryngeal nerve palsy, and 10 had findings suggestive of tracheal invasion. Preoperative radiotherapy and/or chemotherapy was given to 32 low-risk patients.

Results: The hospital mortality rate was 4%. Bowel reconstruction was completed in all cases. No macroscopically recognizable lesion remained after operation in 35 patients. Eight patients were alive 5 years after esophagectomy, including 2 who had had tracheal invasion and 1 with recurrent nerve palsy. The cumulative 5-year survival was 38%.

Conclusions: Evidence of major involvement of the neck and/or upper mediastinum does not always contraindicate resection. Aggressive esophagectomy combined with perioperative adjuvant therapy yielded acceptable palliation and occasional cure in cases with technically resectable lesions. *J. Surg. Oncol.* 1998;67:6–10. © 1998 Wiley-Liss, Inc.

KEY WORDS: carcinoma of the thoracic esophagus; major involvement of the neck or upper mediastinum; surgical treatment for esophageal cancer

INTRODUCTION

In carcinoma of the thoracic esophagus, it is commonly believed that when massive extraesophageal involvement is present in the neck or upper mediastinum, esophagectomy does not benefit patients [1–4]. However, improved quality of life can be anticipated after

esophagectomy, if the macroscopically recognizable carcinoma lesions are all removed and the bowel tract is reconstructed without any serious complication [5]. Re-

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cently, the accuracy of diagnostic imaging has improved considerably [6] and the operative risk of esophagectomy has become acceptable [7]. Therefore, we have attempted radical resection even for patients with extensive involvement in the neck or upper mediastinum, when the lesions were preoperatively assessed as technically resectable and no hematogenic metastasis was detected. In the current study, we analyzed the effect of aggressive operation for such advanced disease.

PATIENTS AND METHODS

We retrospectively investigated results after esophagectomy in thoracic esophageal carcinoma patients who had evidence of extensive involvement in the neck and/or upper mediastinum before treatment, defined as follows: (1) enlarged peritracheal lymph nodes 15 mm or more in diameter demonstrated on computed tomography (CT); (2) cervical lymph nodes assessed as definitely positive by palpation; (3) tracheal invasion strongly suggested by CT or bronchoscopy findings; and (4) recurrent laryngeal nerve palsy. Among patients with carcinoma of the thoracic esophagus treated at our institution from January 1988 to June 1996, 81 had extensive involvement in the neck or upper mediastinum according to the above definitions. Resectability was assessed by physical examination, esophagography, esophagoscopy, cervical and abdominal echography, CT, and bronchoscopy. We attempted esophagectomy with systematic lymph node dissection when the lesions were assessed as technically resectable, excluding cases with metastatic lesions in distant organs or distant lymph nodes, such as the anterior mediastinal, pulmonary hilar, and abdominal periaortic lymph nodes. Deep cervical and cervical peritracheal lymph nodes were not classified in the distant group [7]. Surgery was performed in 44 patients; 2 underwent exploratory operation and 42 esophagectomy. In the current study, these 42 patients who underwent esophagectomy were investigated. During the same period, a total of 364 patients underwent esophagectomy for carcinoma of the thoracic esophagus.

The main tumor was located in the upper third of the esophagus in 18 patients, in the middle third in 20 patients and in the lower third in 4 patients. On preoperative assessment, 32 patients had enlarged peritracheal nodes more than 15 mm in diameter on computed tomography, 18 patients had hard unmobile lymph nodes palpable in the lower neck, 9 patients had recurrent laryngeal nerve palsy and 10 patients had findings which strongly indicated tracheal invasion (tight contact with the tumor mass wider than two fifths of the tracheal circumference with marked deformity or displacement of the tracheal wall). No patients had a tracheoesophageal fistula. The precise sites of palpable tumors in the neck were all identified on CT and echography. Palpable tumors were located in the peritracheal regions in 5 patients, in the

TABLE I. Regimens for Preoperative Adjuvant Therapy for Low-Risk Cases With Major Involvement of the Neck or Upper Mediastinum*

1988–1992
Chemo- and radiotherapy for cases with tracheal invasion
CDDP: 75 mg/m ² , day 1
5-FU: 300 mg/m ² , days 1–28
Radiation: 2 Gy × 5 days/week, for 4 weeks
Chemotherapy for cases without tracheal invasion
CDDP: 75 mg/m ² , day 6
5-FU: 350 mg/m ² , days 1–5
1993–1996
Chemo- and radiotherapy for all cases
CDDP: 7 mg/m ² × 5 days/week, for 4 weeks
5-FU: 200 mg/m ² , days 1–28
Radiation: 2 Gy × 5 days/week, for 4 weeks

*High-risk cases and cases with extensive abdominal involvement were excluded. CDDP, cisplatin; 5-FU, 5-fluorouracil.

deep cervical region lateral to the common carotid artery in 8 patients and in both sites in 5 patients.

Perioperative adjuvant therapy was given when possible. Preoperatively, patients with extensive lymph node involvement were given chemotherapy and those with tracheal invasion were given combined chemo- and radiotherapy through the end of 1992, in principle. From 1993, both groups were treated with chemo- and radiotherapy before operation (Table I). Postoperatively, radiotherapy and/or chemotherapy was given to patients depending on their general physical condition (Table II).

At operation, we routinely performed systematic cervical lymph node dissection before thoracotomy to evaluate the degree of carcinoma extension in the neck and upper peritracheal regions in the earlier phase of the operation [7]. The recurrent laryngeal nerves were identified and isolated during the cervical procedure. To obtain a sufficient operative view of the thoracocervical junction, middle sternotomy was carried out in 20 cases, and the upper part of the manubrium sterni was resected in 15 cases. In four cases with extensive involvement around the angle of the right internal jugular and subclavian veins, the right clavicle was partly removed or temporarily mobilized with a part of the first rib and manubrium. Thoracotomy was made on the right side, excluding the following three patients, who were operated on by left thoracotomy. One had previously undergone left thoracoplasty and left thoracotomy was selected because of his impaired pulmonary function. The other two patients had extensive upper abdominal involvement immediately beneath the hiatus for which a left thoracoabdominal incision provided a wider operative view. Of 10 cases with tracheal invasion, the tracheal wall was partially resected in 8 and the upper part of the trachea was removed with the larynx in 2 cases.

The operation was defined as curative when no macroscopically recognizable carcinoma lesion remained, re-

TABLE II. Perioperative Adjuvant Therapy for Cases With Major Involvement of the Neck or Upper Mediastinum

	No. of patients	
	Preoperative	Postoperative
None	10	14
Radiation	2	8
Chemotherapy	10	12
Chemo- and radiotherapy	20	8

gardless of the microscopic findings of the resection margin [8]. The resected esophagus and lymph nodes were all examined histopathologically. The preoperative therapy was evaluated as effective, when less than one-third of the carcinoma lesion remained in the esophagus on histopathological assessment.

Survival curves were made by the Kaplan–Meier method. The difference in survival was evaluated by the logrank method.

RESULTS

Of 42 patients who underwent esophagectomy, 2 patients (4%) died during hospitalization. Both died of carcinoma recurrence. The operation was judged to be curative in 35 patients. Of the other 7 patients, resection was incomplete due to carcinoma infiltration of the pharynx in 3, extensive involvement of distant lymph nodes in 2, pulmonary metastasis in 1, and infiltration of the left main bronchus in 1 patient.

No patients had fatal postoperative complications (Table III). Either recurrent laryngeal nerve was resected in 9 cases due to massive carcinoma infiltration. Palsy of the preserved recurrent nerve developed in 10 cases. Although hoarseness persisted in the former group of patients, it disappeared within several months in all but one of the latter group of patients. In all patients who developed anastomotic leakage, the bowel continuity was restored before discharge from the hospital.

Preoperative adjuvant therapy was histopathologically judged to be effective for the primary esophageal tumor in 12 cases, 2 of which had no residual carcinoma cells in the resected specimens. All lymph nodes in the neck or upper mediastinum preoperatively assessed as definitely positive presented histopathological evidence of current or previous involvement, except in the following 2 cases after effective preoperative therapy. One had small cell carcinoma and an enlarged lymph node in the right peritracheal region 22 mm in diameter demonstrated on CT before treatment, which markedly decreased in size after chemotherapy. The other had left recurrent laryngeal nerve palsy and an ill-defined left peritracheal lesion 24 mm in diameter on CT, which was macroscopically identified as a hard fibrotic tumor involving the left recurrent laryngeal nerve at operation after chemo- and radiotherapy. In all cases in which tracheal invasion was

TABLE III. Major Postoperative Complications After Esophagectomy in Patients With Major Involvement of the Neck or Upper Mediastinum

Complication	No. of patients
Palsy of preserved recurrent laryngeal nerve	10
Anastomotic leakage	6
Tracheal ischemia	4
Pneumonia	2
Sternal infection	2

strongly suspected before treatment, carcinoma cells or granulomas caused by carcinoma necrosis were microscopically found in the resected tracheal wall or margin of the tracheal resection.

After esophagectomy, 13 patients survived more than 2 years and 8 were alive at 5 years; the cumulative 5 year survival rate was 38%. The 5-year survivors included 2 patients with tracheal invasion and one with recurrent nerve palsy before operation. All patients in whom resection was incomplete died within 1 year, compared with the 5-year survival rate of 45% in patients who were able to undergo curative resection (Fig. 1). In the subgroup with palpable involved lymph nodes in the neck, the 5-year survival was 34% (Fig. 2). Patients in whom preoperative therapy had been effective had a significantly more favorable outcome: the 5-year survival rate was 69%, compared with 28% in other patients who received preoperative therapy ($P < 0.05$) (Fig. 3).

Carcinoma recurrence was clinically confirmed in 15 patients after curative operation. The pattern of carcinoma recurrence was locoregional in 4 patients, hematogenous in 9, and mixed in 2. Locoregional recurrence in the neck or upper mediastinum was found in 2 patients.

DISCUSSION

In carcinoma of the thoracic esophagus, it has been reported that lymph nodes located beside the recurrent laryngeal nerves and in the cervical base are frequently involved from the early phase of carcinoma invasion, and that, therefore, these nodes should not be considered as distant lymph nodes [7,9]. We have also reported that outcomes after esophagectomy in cases in which these nodes were involved were not necessarily unfavorable [7]. Therefore, even when patients have markedly massive extraesophageal carcinoma invasion to the neck or upper mediastinum, it is still possible that systemic carcinoma dissemination is not markedly extensive. Our results in the present series demonstrated that aggressive esophagectomy benefited a proportion of patients with such advanced disease, including those who had enlarged unmobile tumors palpable in the neck, recurrent laryngeal nerve palsy, or tracheal invasion.

Although the cervical and upper peritracheal lymph

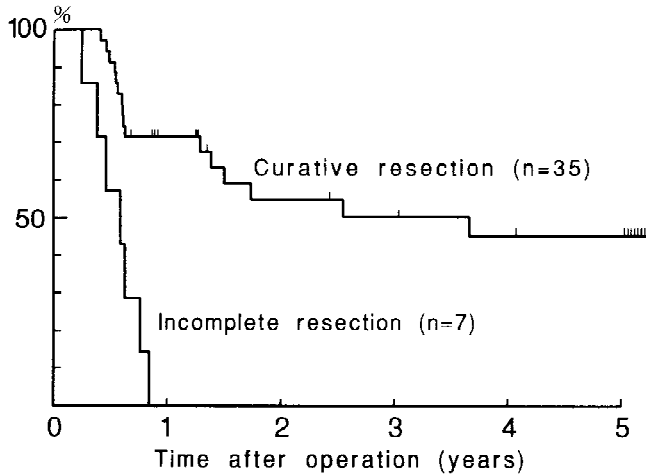


Fig. 1. Cumulative survival curves after esophagectomy in cases with major involvement of the neck or upper mediastinum related to operative curability. The difference was significant ($P = 0.0001$). n, number of patients.

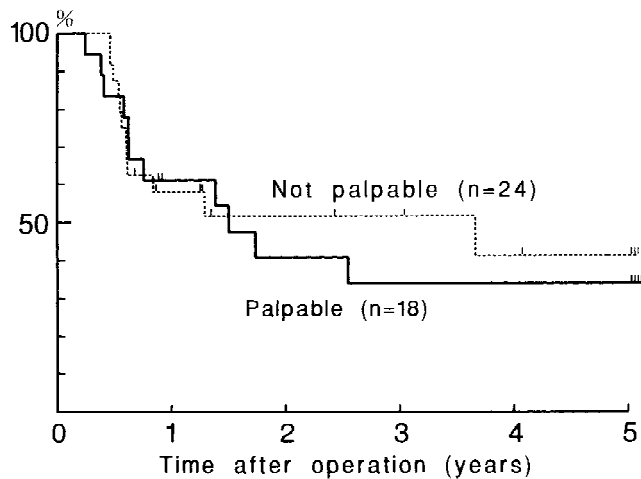


Fig. 2. Cumulative survival curves in cases with and without carcinoma involvement definitely palpable in the neck. Both groups presented similar outcomes. n, number of patients.

nodes are classified in different categories by the UICC TNM classification [10], major involvement of these nodes had similar clinical significance. Cervical and mediastinal peritracheal regions are located continuous to each other without a definite border. Massive tumor infiltration in the mediastinal peritracheal region often presents a palpable cervical mass, and palpability varied depending on the patient's physical constitution. The patient group with palpable cervical mass showed no poorer outcome than the other patients in this study.

To select candidates for operation, the spread of the disease should be accurately assessed before treatment. Although the sensitivity of preoperative assessment of carcinoma invasion has limitations, definite positive findings are reliable [6]. In this series, cervical and up-

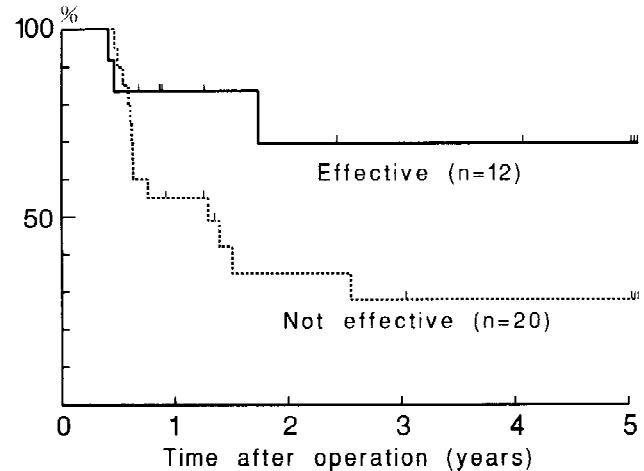


Fig. 3. Cumulative survival curves in patients receiving preoperative therapy in relation to the histopathological effect. The patients in whom preoperative therapy had been effective had a significantly more favorable outcome ($P < 0.05$).

per-mediastinal findings assessed as definitely positive proved correct on histopathological examination after esophagectomy in all but two cases, in which preoperative therapy seemed to have totally erased the histopathological evidence.

Since the mortality rate following aggressive esophagectomy has recently decreased to acceptable levels and curative resection offers a relatively favorable outcome with improved quality of life [5,6,8,11], it is more important not to exclude patients with resectable carcinoma from operation than to avoid operation for unresectable disease. Therefore, we operated upon patients unless the disease was assessed as absolutely unresectable for technical reasons or due to distant metastasis. With such a liberal standard for selection of operative candidates, the resectability rate was high and macroscopically recognizable carcinoma lesions remained in only 20% of patients operated upon in this series. These results suggest that patients who would benefit from esophagectomy could be selected with acceptable accuracy.

It is highly probable that patients with extensive local carcinoma invasion also have microscopic systemic dissemination. However, results were considerably more favorable when entire macroscopically detectable carcinoma lesions could be removed, compared with unfavorable outcomes in cases with macroscopically incomplete resection. Most patients who survived more than three years had received perioperative chemotherapy. These results suggest that, when macroscopically detectable lesions can be removed by operation, microscopic dissemination of carcinoma cells is considerably better controlled by adjuvant therapy [12]. The patient group in which preoperative therapy was effective had a relatively better outcome.

CONCLUSION

Definite evidence of extraesophageal involvement of the lower cervical or peritracheal regions does not always contraindicate esophagectomy. Aggressive esophagectomy with proper adjuvant therapy yielded good palliation and occasional cure, when no macroscopically detectable lesion remained after the operation. Patients who would benefit from esophagectomy could be selected by preoperative diagnostic imaging with acceptable accuracy.

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